REMARKS

After entry of this amendment, claims 12-15 and 19-59 are currently pending in the instant application. Claims 12-15 and 19-54 have been withdrawn. New claims 55-59 have been added. Support for new claims 55-59 can be found throughout the specification and claims. Support for claim 55 can be found, *inter alia*, at page 4, lines 13-21, page 7 , line 10 to page 8, line 6, and Example 2, pages 17-19. Support for claim 56 can be found, *inter alia*, at page 9, lines 2-7 and Example 2.8, pages 24-25. Support for claim 57 can be found, *inter alia*, at page 9, lines 7-13 and Example 2.9, pages 25-28. Support for claim 58 can be found, *inter alia*, at Example 1, pages 13-17. Support for claim 59 can be found, *inter alia*, at page 6, lines 9-11.

Correspondence between old claims 1-8, 10, 11, and 16-18 and new claims 55-59 is shown below:

Old Claims	New Claims
1+2+10+11+16+17+18	55
8	56
7	57
-	58
-	59

Old claims 3-6 have been canceled with no new counterparts.

No new matter has been added.

Sequence Compliance

The Examiner has indicated an unidentified amino acid sequence within the specification.

In response, Applicants have amended the specification at page 26 to identify said amino acid sequence with the proper sequence identifier, *i.e.*, SEQ ID NO:13 and submit herewith a Substitute Sequence Listing in paper and computer readable form which contains the sequence information for SEQ ID NO:13. Support for the

amendment can be found in the specification, as filed. The Substitute Sequence Listing contains no new matter.

In light of the above amendments and remarks, Applicants submit that the sequence disclosures are in compliance. Thus, this objection has been overcome.

Specification/Informalities

The Examiner contends that the title of the invention is not descriptive of the invention to which the claims are directed.

In response, Applicants have amended the title to correspond to the preamble of new claim 55.

In light of the above amendments and remarks, Applicants submit that the title is indicative of the invention as claimed. Thus, this objection has been overcome.

Claim Objections

Claims 1, 2, 5, 6, and 10 are objected to for containing abbreviations without at least once reciting the entire phrase for which the abbreviation is used.

As a preliminary matter, Applicants point out that claims 1, 2, 5, 6, and 10 have been canceled. New claim 55 recites "p21-activated kinase 2" for which the abbreviation "PAK2" is used. New claim 58 recites "chronic obstructive pulmonary disease" for which the abbreviation "COPD" is used.

Applicants submit that the abbreviations in new claims 55-59 are recited in their entireties at least once; thus, this objection is moot.

Rejections under 35 U.S.C. §112, Second Paragraph

Claims 1-8, 10, 11, and 16-18 are rejected under 35 U.S.C. §112, second paragraph as being indefinite.

As a preliminary matter, Applicants point out that claims 1-8, 10, 11, and 16-18 have been canceled.

Claims 1 and 2 (and claims 3-8, 10, 11 and 16-18 dependent thereon) are rejected as being incomplete for lacking correlation between method steps (a) and (b) and whether the substance is an activator or inhibitor.

Applicants point out that that new claim 55 (and claims 56-59 dependent thereon) recite "wherein a substance which activates said substrate phosphorylation or substrate recognition or substrate binding is a substance which can be used to inhibit or to reduce a chronic inflammatory airway disease in which a macrophage is in a hyperactivated status due to down-regulated PAK2 kinase." Applicants submit that new claim 55 (and claims 56-59 dependent thereon) recite a correlation between method steps (a) and (b) and whether the substance inhibits or reduces a chronic inflammatory airway disease.

Claims 1 and 2 (and claims 5-8, 10, and 11) and claims 3 and 4 are rejected as being indefinite in the recitation of the term "function."

Applicants point out that new claims 55-59 do not recite the term "function." New claim 55 (and claims 56-59 dependent thereon) recite specific biological activities, *i.e.*, "substrate phosphorylation or substrate recognition or substrate binding" of PAK2.

Claims 1 and 2 (and claims 3-8 and 16-18 dependent thereon) are rejected as being indefinite in the recitation of "PAK2".

According to the Examiner, the specification fails to teach which identifying characteristics distinguish a PAK2 from other serine/threonine kinases.

New claim 55 (and claims 56-59 dependent thereon) recites a PAK2 kinase having an amino acid sequence as depicted in SEQ ID NO:4 or an equivalent, variant, mutant or fragment of the PAK2 kinase *having substrate phosphorylation or substrate recognition or substrate binding capability thereof.* Applicants submit that the skilled artisan know how to create equivalents, variants, mutants or fragments of the PAK2 kinase. Further, methods for determining biological activity of the equivalents,

variants, mutants or fragments of the PAK2 kinase are well-known in the art. For example, determining whether the equivalent, variant, mutant or fragment can bind to a substrate can be done using well-known gel-shift analysis.

Claims 3 and 4 are rejected as being indefinite in the recitation of "measured directly" or "measured indirectly", respectively.

Applicants submit that claims 3 and 4 have been canceled; thus, this rejection is overcome with respect to these claims.

Claim 10 has been rejected as being indefinite due to its dependency upon claim 2.

Applicants point out that new claim 55 which corresponds, in part, to claim 10, now canceled, recites a PAK2 kinase having an amino acid sequence as depicted in SEQ ID NO:4 or an equivalent, variant, mutant or fragment of the PAK2 kinase. Applicants submit that claim 55 is clearly defined.

Claim 11 has been rejected as being indefinite due to its dependency upon claim 10.

Applicants point out that new claim 55 which corresponds, in part, to claim 11, now canceled, recites a PAK2 kinase having an amino acid sequence as depicted in SEQ ID NO:4 or an equivalent, variant, mutant or fragment of the PAK2 kinase. Applicants submit that claim 55 is clearly defined.

Applicants respectfully submit that in view of the above amendments and remarks, all the rejections under 35 U.S.C. §112, second paragraph have been overcome and ust be withdrawn.

Rejections under 35 U.S.C. §112, First Paragraph

Claims 1-8, 11, and 16-18 are rejected under 35 U.S.C. §112, first paragraph for lack of written description.

The Examiner contends that there is a lack of description of a representative number of PAK2 polypeptides. Furthermore, regarding claims 5 and 6, the Examiner

contends that the specification fails to provide characteristics that distinguish a "mammalian" or "human" PAK2 polypeptide from those PAK2 proteins that are not "mammalian" or "human".

As a preliminary matter, Applicants point out that claims 1-8, 11, and 16-18 have been canceled. Claims 3-6 have no new counterpart.

New claim 55 (and claims 56-59 dependent thereon) recites a method comprising contacting a PAK2 kinase having an amino acid sequence as depicted in SEQ ID NO:4 or an equivalent, variant, mutant or fragment of the PAK2 kinase having substrate phosphorylation or substrate recognition or substrate binding capability thereof. Thus, new claim 55 (and claims 56-59 dependent thereon) recite sequence information and biological characteristics.

Applicants submit that in view of the amendments and remarks, this rejection under Section 112, first paragraph for lack of written description has been overcome and must be withdrawn.

Claims 1-8, 10 11, and 16-18 are rejected under 35 U.S.C. §112, first paragraph for lack of enablement.

The Examiner contends that the specification, while being enabling for a method for determining whether a substance is an activator or inhibitor of the kinase activity of SEQ ID NO:4, does not reasonably provide enablement for a method for determining whether a substance is an activator or inhibitor of any function of all PAK2 proteins, including variants, mutants, and fragments thereof.

As a preliminary matter, Applicants point out that claims 1-8, 10, 11, and 16-18 have been canceled. Claims 3-6 have no new counterpart.

New claim 55 (and claims 56-59 dependent thereon) recites a method comprising contacting a PAK2 kinase *having an amino acid sequence as depicted in SEQ ID NO:4 or an equivalent, variant, mutant or fragment of the PAK2 kinase having*

substrate phosphorylation or substrate recognition or substrate binding capability thereof. Thus, new claim 55 (and claims 56-59 dependent thereon) recite sequence information and biological characteristics. As mentioned above, methods for determining biological activity of the equivalents, variants, mutants or fragments of the PAK2 kinase having an amino acid sequence as depicted in SEQ ID NO:4 are well-known in the art. For example, determining whether the equivalent, variant, mutant or fragment can bind to a substrate can be done using well-known gel-shift analysis. Thus, undue experimentation is not required.

Applicants submit that in view of the amendments and remarks, this rejection under Section 112, first paragraph for lack of enablement has been overcome and must be withdrawn.

Applicants submit that in view of the amendments and remarks, all of the rejections under Section 112, first paragraph have been overcome and must be withdrawn.

Rejections under 35 U.S.C. §102

Claims 1-6, 8, 10, 11, and 16-18 are rejected under 35 U.S.C. §102(b) as being anticipated by Benner *et al.*, J. Biol. Chem. 270:21121-21128 ("Benner *et al.*").

Claims 1-8, 11, and 16-18 are rejected under 35 U.S.C. §102(b) as being anticipated by Lee *et al.*, PNAS 94:13642-13647 ("Lee *et al.*").

As a preliminary matter, Applicants point out that claims 1-8, 10, 11, and 16-18 have been canceled. Claims 3-6 have no new counterpart.

The Cited References

According to the Examiner, Benner *et al.* teach methods for assaying the effects of trypsin and magnesium on the activity of a kinase synonymous with PAK2 kinase.

According to the Examiner, Lee *et al.* teach a method for assaying the effects of Fas-induced apoptosis and caspase cleavage on the activation of human PAK65/PAK2 and a deletion fragment thereof.

Novelty of the Present Claims

New claim 55 (and claims 56-59 dependent thereon) recites a method for determining whether a substance inhibits or reduces a chronic inflammatory airway disease in which a macrophage is in a hyperactivated status due to down-regulated p21-activated kinase 2 (PAK2) kinase comprising contacting a PAK2 kinase having an amino acid sequence as depicted in SEQ ID NO:4 or an equivalent, variant, mutant or fragment of the PAK2 kinase having substrate phosphorylation or substrate recognition or substrate binding capability thereof... *wherein a substance which activates said substrate phosphorylation or substrate recognition or substrate binding is a substance which can be used to inhibit or to reduce a chronic inflammatory airway disease in which a macrophage is in a hyperactivated status due to down-regulated PAK2 kinase.*

Applicants submit that the present invention discloses that hyperactivated macrophages are the discriminating feature between healthy smokers and smokers suffering from chronic obstructive pulmonary disease (COPD) (*See* page 4, lines 13-17 of the specification). Additionally, the present invention discloses a link between phenotypic changes in macrophages due to differentially expressed proteins (*See* page 5, lines 13-21 of the specification). Further, it was identified that PAK2 is a protein kinase which is linked to the hyperactivated phenotype of macrophages which again is linked to chronic inflammatory airway diseases (*See* page 6, line 23 to page 7, line 8 and Example 1, pages 13-17 of the specification). These findings provide the basis for a method for determining whether a substance inhibits or reduces a chronic inflammatory airway disease in which a macrophage is in a hyperactivated status due to down-regulated PAK2 kinase. Therefore, the present invention does not deal with trivial assays for determining whether a substance is an activator or inhibitor of PAK2 kinase.

In light of the above amendments and remarks, Applicants respectfully submit that the cited references cannot and do not anticipate the claimed methods. Accordingly, the rejections based on Section 102(a) must be withdrawn.

CONCLUSION

In light of the above amendments and remarks, Applicants submit that all of the objections and rejections have been overcome and must be withdrawn. Further, Applicants submit that the application is now in form for issuance and an early allowance is earnestly requested. If any issues remain, the Examiner is invited to telephone the Attorney at the number below

Respectfully submitted,

Susan K. Pocchiari

Susan K. Pocchiari
Registration No. 45,016
Attorney for Applicants

BOEHRINGER INGELHEIM CORPORATION
Patent Department
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877
(203) 798-5648
(203) 798-4408

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Susan K. Pocchiari

Susan K. Pocchiari
Registration No. 45,016